Interview Summary

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Dated: February 8, 2010 Electronic Signature for Thomas J. Engellenner: /Thomas J. Engellenner/

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Anthony Atala et al.

Application No.: 10/766,642 Confirmation No.: 4621

Filed: January 28, 2004 Art Unit: 1651

For: ENHANCEMENT OF ANGIOGENESIS TO GRAFTS USING CELLS ENGINEERED TO PRODUCE GROWTH FACTORS Examiner: Allison M. Ford

Commisioner for Patents
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Alexandria, VA 22313-1450

INTERVIEW SUMMARY

Dear Sir:

In connection with a personal interview on February 2, 2010 with Examiner Ford in the above-referenced patent application, Applicants provide the following remarks.

Interview Summary and Remarks begin on Page 2.

INTERVIEW SUMMARY AND REMARKS

Applicants' representative, Thomas Engellenner, attorney of record, thanks Examiner Ford for the courtesy of an interview on February 2, 2010 to discuss the present application.

Applicants' representative noted that the present invention is directed to a method of organ augmentation that utilizes two populations of transplanted cells with distinct functions, a *first population of cells* that is *transiently transfected* to express an *angiogenesis modulating agent*, and a *second population of cells to be assimilated* at the target site. Independent claim 1 is directed to a method of organ augmentation using the two populations of cells, implanted together in an *injectable polymer matrix*. Independent claim 23 is directed to a method that involves implanting the two populations cells in an *organ construct*. Preferably, the transfected cells of the first population are also *encapsulated* to immunoisolate the cells from the target tissue into which they are injected or implanted (as recited in claims 10 and 33).

The recently filed response (dated January 4, 2010) was discussed. Applicants' representative noted that only issues in this case were rejections based on purported obviousness over US Patent Application Pub. No. 2003/0007954 (Naughton) together with various combinations of five (or more) additional references. It was argued that the combination of such a large number of references suggested impermissible hindsight reconstruction of the invention.

More fundamentally, however, Applicants' representative stressed that the principal reference, Naughton, clearly taught away from the combinations constructed by the Examiner insofar as the claimed invention was based on the use of cells genetically engineered to *transiently* produce an angiogenesis modulating agent.

It was noted that Naughton teaches the advantages of three-dimensional stromal tissue implants that constituently produce angiogenesis factors. Naughton's stromal cells are *fibroblasts* and other cells obtained from connective tissue biopsies. Naughton states, for example, in

paragraph [0010] that "three-dimensional stromal tissue implants secrete a variety of growth factors critical to tissue regeneration and angiogenesis."

However, Naughton fails to teach or suggest using two separate populations of cells, *transiently transfecting* a first population to express the angiogenesis modulating agent VEGF and delivering the two populations together such that the *transient expression of the angiogenesis modulating agent by the first population of cells* promotes the *assimilation and differentiation of the second population of cells at the target region.*

In fact, the Naughton reference actually *teaches away* from the present invention. Specifically, at page 1, paragraph [0006], Naughton teaches:

> Recently, a gene-therapy approach was used to deliver VEGF by injection of retroviral vectors that targeted heart tissue and resulted in VEGF production (Losordo et al., 1998, Circulation 98:2800-2804). This in situ method improved blood flow and subjective symptoms in patients, suggesting that local delivery of a growth factor such as VEGF to promote angiogenesis in heart tissues may be of therapeutic value in the treatment of certain heart conditions. *However, such gene therapy techniques utilizing retroviral vectors present certain inherent risks and safety concerns.* In addition, gene therapy-type approaches present a number of *unresolved, problematic technical hurdles such as low transfection levels for recipient cells, construct instability and long-term expression of the desired gene product from the transfected cells.* (Emphasis added)

Naughton clearly rejects the approach of using transfected cells to express angiogenesis modulating agents, such as VEGF. In fact, Naughton's principal contribution to the art lies in teaching that a three-dimensional stromal tissue bed, preferably including fibroblasts, will intrinsically express and secret VEGF. Thus, one skilled in the art would not have been lead to supplement Naughton's construct with a *separate* population of cells *genetically engineered* to express angiogenesis modulating agents. Given this negative teaching, there would be no reason to combine Naughton with any of the secondary references to reconstruct the present invention.

Moreover, Naughton's use of *three dimensional* constructs further teaches away from the methods of claim 1, which recites a method in which the first and second populations of cells are suspended in a*n injectable polymer matrix.* In contrast, Naughton describes her three dimensional

construct as a "*framework composed of a biocompatible, non-living material formed into a three-dimensional structure having interstitial spaces bridged by the stromal cells.*" See, Naughton at paragraph [0025]. Again, in light of this contrary teaching, there would be no reason to combine Naughton with any of the secondary references to reconstruct the the present invention.

It was further argued that dependent claims 10 and 33 (which recite techniques for encapsulating the transiently transfected first population of cells) were patentable because one skilled in the art would not have been lead to supplement Naughton's construct with a *separate* population of cells *genetically engineered* to ***transiently*** express angiogenesis modulating agents, and *encapsulated* to provide immunoisolation.

In addition to arguing the patentability of the pending amended claims, Applicants' representative also pointed out several additional inventive features recited in the new claims that were presented in the January 4, 2010 submission. Specifically, new claims 38-43 in which preferred cell types for applicant's first and cell populations are recited, e.g., *endothelial progenitor cells* and *myoblasts*. Naughton neither teaches nor suggests any advantages for such cell types and, again teaches away from the present invention by reliance on *fibroblast* based constructs.

The Examiner was also invited to call Applicants' representative following her review of Applicants' response to discuss any remaining issues or to suggest any further claim amendments that might be deemed necessary or desirable for allowance.

CONCLUSION

In view of the above remarks, and the arguments presented in more detail in their December 22, 2010 response, Applicants again respectfully request reconsideration and allowance of this application.

Respectfully submitted,

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